

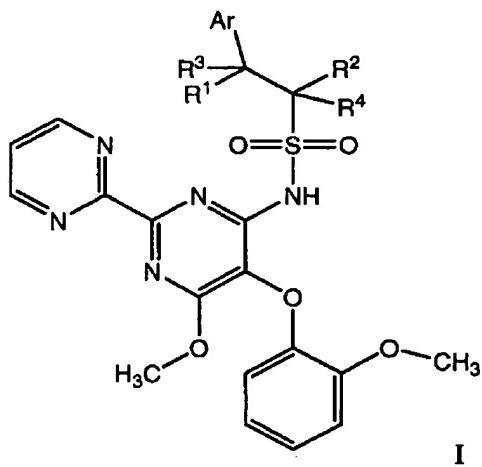
PATENT/Docket No. PC10901A  
 Appl. No. 09/779,413  
 Filing Date: February 8, 2001  
 Response dated October 1, 2004  
 Response to Office Action of July 29, 2004

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1. (Currently amended) A method for the treatment or prophylaxis of an endothelin-mediated disorder in a companion animal which comprises administering an effective amount, wherein the free blood plasma concentration after twenty four hours remains above the concentration providing efficacy for said endothelin-mediated disorder, of a compound of formula I or a veterinarian acceptable salt thereof to the companion animal, compound of formula 1 having the formula:



wherein R<sup>1</sup> and R<sup>2</sup> each represent H, or together represent a second carbon-carbon bond between the carbon atoms to which they are attached;

when R<sup>1</sup> and R<sup>2</sup> each represent H, then R<sup>3</sup> and R<sup>4</sup> also represent H;

when R<sup>1</sup> and R<sup>2</sup> together represent a second carbon-carbon bond between the carbon atoms to which they are attached, then R<sup>3</sup> and R<sup>4</sup> independently represent H or C<sub>1</sub>-C<sub>6</sub> alkyl;

Ar represents:

phenyl or naphthyl, which groups are optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl (~~which may itself be substituted by one or more substituents selected~~

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from halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl) and N((C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>), halo, C<sub>1</sub>-C<sub>6</sub> alkoxy,

CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), N(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>, OH and C<sub>1</sub>-C<sub>3</sub>

alkylene dioxy and CF<sub>3</sub>, or

— a 5 or 6 membered heteroaryl ring containing up to 4 heteroatoms selected from N, O and S, which group is optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), and N(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>.

2. (Previously presented) A method according to claim 1, wherein the companion animal is a cat, a dog or a horse.

3. (Previously presented) A method according to claim 1 or 2, wherein the endothelin mediated disorder is hypertension, congestive heart failure or chronic renal failure.

4. (Previously presented) A method according to claim 1, wherein R<sup>1</sup> and R<sup>2</sup> each represent H.

5. (Previously presented) A method according to claim 1, wherein R<sup>3</sup> and R<sup>4</sup> each represent H.

6. (Canceled)

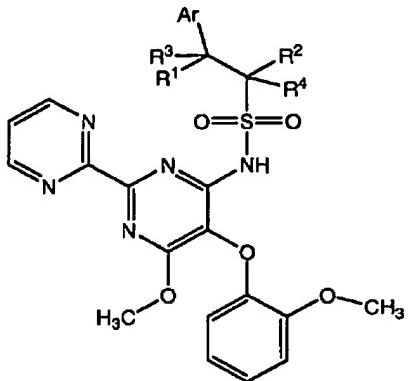
7. (Previously presented) The method according to claim 1, wherein Ar is phenyl.

8. (Previously presented) The method of claim 1, wherein the endothelin mediated disorder is congestive heart failure.

9. (Previously presented) The method of claim 1, wherein the endothelin mediated disorder is chronic renal failure.

10. (Currently amended) A formulation containing a compound of formula I or a veterinarily acceptable salt thereof:

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wherein R<sup>1</sup> and R<sup>2</sup> each represent H, or together represent a second carbon-carbon bond between the carbon atoms to which they are attached;

when R<sup>1</sup> and R<sup>2</sup> each represent H, then R<sup>3</sup> and R<sup>4</sup> also represent H;

when R<sup>1</sup> and R<sup>2</sup> together represent a second carbon-carbon bond between the carbon atoms to which they are attached, then R<sup>3</sup> and R<sup>4</sup> independently represent H or C<sub>1</sub>-C<sub>6</sub> alkyl;

Ar represents:

phenyl or naphthyl, which groups are optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl (which may itself be substituted by one or more substituents selected from halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl) and N((C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>), halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), N(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>, OH and C<sub>1</sub>-C<sub>3</sub> alkylene dioxy and CF<sub>3</sub>, or

~~a 5 or 6 membered heteroaryl ring containing up to 4 heteroatoms selected from N, O and S, which group is optionally substituted by one or more groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halo, C<sub>1</sub>-C<sub>6</sub> alkoxy, CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, NO<sub>2</sub>, CN, NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), and N(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>,~~

the formulation characterized in that it is suitable for administration to a companion animal, wherein the free blood plasma concentration of compound of formula 1 after twenty four hours remains above the concentration providing efficacy for said endothelin-mediated disorder.

11. (Previously presented) A formulation according to claim 10, which is suitable for oral administration to the companion animal.

12-14. (Canceled)

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15. (New) A method according to claim 1 wherein the compound of formula 1 is N-[6-methoxy-5-(2-methoxyphenoxy)-2-(2-pyrimidinyl)-4-pyrimidinyl]-2-phenylethanesulfonamide.

16. (New) A method according to claim 1 wherein the compound of formula 1 is N-[6-methoxy-5-(2-methoxyphenoxy)-2-(2-pyrimidinyl)-4-pyrimidinyl]-2-phenylethanesulfonamide.

17. (New) A formulation according to claim 10 wherein the compound of formula 1 is N-[6-methoxy-5-(2-methoxyphenoxy)-2-(2-pyrimidinyl)-4-pyrimidinyl]-2-phenylethanesulfonamide.

18. (New) A formulation according to claim 10 wherein the compound of formula 1 is N-[6-methoxy-5-(2-methoxyphenoxy)-2-(2-pyrimidinyl)-4-pyrimidinyl]-2-phenylethanesulfonamide.